Departement für Kleintiere, Klinik für Kleintiermedizin
der Vetsuisse-Fakultät Universität Zürich

Direktorin: Prof. Dr. med. vet. Claudia Reusch

Arbeit unter wissenschaftlicher Betreuung von
Frau Prof. Dr. med. vet. Nadja Sieber-Ruckstuhl

# Effects of the Contrast Medium Injection Technique on Attenuation Values of Normal Adrenal Glands in Dogs during Contrast-Enhanced Computed Tomography

**Inaugural-Dissertation**

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vorgelegt von

**Alexandra Blaser**

Tierärztin
von Wettingen

genehmigt auf Antrag von

Prof. Dr. med. vet. Nadja Sieber-Ruckstuhl, Referentin

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# Summary

**Objective-** To compare the effects of 3 contrast medium injection protocols on attenuation values of the adrenal glands in dogs.

**Animals-** 9 healthy Beagles.

**Procedures-** Multislice CT scans were carried out before and at 19 time points after contrast medium injection. Following protocols were evaluated in a randomized cross-over trial: 700 mg iodine/kg at constant injection rate over 20 s (full constant (FC)), 700 mg iodine/kg following an exponential decay curve over 20 s (full exponential (FE)) and 350 mg iodine/kg at constant injection rate over 10 s (half constant (HC)).

Results- Peak attenuation (median) was 129 Hounsfield units (HU), 133 HU and 87 HU for injecting at FC, FE and HC rates, respectively. Peak attenuation differed significantly between FC and HC injections and between FE and HC injections. Time to peak attenuation (median) did not differ significantly between injection methods and was 30 s, 23 s and 15 s in FC, FE and HC injections, respectively.

**Conclusions and Clinical Relevance-** Dose of contrast medium and timing of scanning, but not injection technique, affect peak attenuation values in adrenal glands. The exponential injection method was complex and seemed prone to error. A constant injection protocol using 700 mg iodine/kg and scanning approximately 30 s after contrast injection provides images with maximum adrenal attenuation values in healthy dogs.



Keywords: adrenals, contrast medium, CT, dog

# Zusammenfassung

**Ziel-** Die Pharmakokinetik von 3 verschiedenen Kontrastmittel-Injektionsprotokollen bei Nebennieren von Hunden zu untersuchen.

**Tiere-** 9 gesunde Beagles.

**Studienaufbau-** Computertomographie(CT)-Bilder wurden vor und an neunzehn Zeitpunkten nach Kontrastmittelinjektion aufgenommen. In der randomisierten cross-over Studie wurden folgende Protokolle evaluiert: 700 mg Iod/kg über 20 Sek in konstanter Injektionsrate (ganze Dosis konstant (GK)) und in exponentieller Injektionsrate (ganze Dosis exponentiell (GE)) sowie 350 mg Iod/kg über 10 Sek in konstanter Injektionsrate (halbe Dosis konstant (HK)).

**Resultate-** Die maximale Attenuierung (Median) bei GK betrug 129 HU und wurde nach 30 Sek (Median) erreicht. Für GE betrugen die Werte 133 HU nach 23 Sek und für HK 87 HU nach 15 Sek. Die Werte der maximalen Attenuierung der GK und der GE unterschieden sich signifikant von der HK. Die Zeit bis zur maximalen Attenuierung unterschied sich nicht signifikant zwischen den Protokollen.

**Schlussfolgerung und klinische Relevanz-** Die Dosis des Kontrastmittels sowie der Messzeitpunkt, jedoch nicht die Injektionstechnik, beeinflussen die maximale Attenuierung der Nebennieren. Die exponentielle Injektionsrate ist komplex und fehleranfällig. Bei konstanter Injektionsrate von 700 mg Iod/kg und Aufnahmen nach 30 Sek ist die maximale Attenuierung der Nebennieren bei gesunden Hunden garantiert.


Schlüsselwörter: Nebennieren, Kontrastmittel, CT, Hund

# Effects of contrast medium injection technique on attenuation values of adrenal glands in healthy dogs during contrast-enhanced computed tomography

**Alexandra Blaser** MVetMed
**Matthias Dennler** Dr Med Vet
**Martina Mosing** Dr Med Vet
**Thomas C. Gent** PhD
**Guido Santner**
**Sandro Imhasly** PhD
**Felicitas S. Boretti** Dr Med Vet
**Claudia E. Reusch** Dr Med Vet
**Patrick Kircher** Dr Med Vet
**Nadja S. Sieber-Ruckstuhl** Dr Med Vet

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From the Clinic for Small Animal Internal Medicine (Blaser, Boretti, Reusch, Sieber-Ruckstuhl), Section of Diagnostic Imaging (Dennler, Kircher), Anaesthesiology Section (Mosing, Gent), and Institute of Pharmacology and Toxicology (Imhasly), Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, 8057 Zurich, Switzerland. Dr. Gent's present address is Centre for Experimental Neurology, Inselspital, University of Bern, 3010 Bern, Switzerland.

Address correspondence to Dr. Sieber-Ruckstuhl (nsieber@vetclinics.uzh.ch).

**OBJECTIVE**
To assess the effects of 3 contrast medium injection techniques on attenuation values for canine adrenal glands during contrast-enhanced CT.

**ANIMALS**
9 healthy Beagles.

**PROCEDURES**
3 protocols were evaluated in a randomized cross-over design study: 700 mg of iodine/kg at a constant injection rate over 20 seconds (full-dose constant rate), the same dose at a rate following an exponential decay curve over 20 seconds (full-dose decelerated rate), and 350 mg of iodine/kg at a constant injection rate over 10 seconds (half-dose constant rate). Multislice CT images were obtained before and at predetermined time points after the start of contrast medium injection.

**RESULTS**
Median peak attenuation values were 129, 133, and 87 Hounsfield units with the full-dose constant rate, full-dose decelerated rate, and half-dose constant rate injection protocols, respectively. Peak attenuation differed significantly between the full-dose constant rate and half-dose constant rate injection protocols and between the full-dose decelerated rate and half-dose constant rate injection protocols. Median time to peak attenuation did not differ significantly among injection methods and was 30, 23, and 15 seconds for the full-dose constant rate, full-dose decelerated rate, and half-dose constant rate injections, respectively.

**CONCLUSIONS AND CLINICAL RELEVANCE**
The dose of contrast medium and the timing of postinjection CT scanning were main determinants of peak attenuation for adrenal glands in healthy dogs; effects of the 3 injection protocols on attenuation were minor. The exponentially decelerated injection method was subjectively complex. A constant injection protocol delivering 700 mg of iodine/kg over 20 seconds, with scans obtained approximately 30 seconds after starting contrast medium injection, provided images with maximum adrenal gland attenuation values. (*Am J Vet Res* 2016;77:144–150)

Contrast-enhanced CT has been used with increasing frequency in veterinary medicine to evaluate various organs and disease processes. The pharmacokinetics of the contrast medium determines the optimal time period for image generation because image acquisition should coincide with the time of highest contrast concentration in the target area and the time of maximum difference in attenuation values between healthy and diseased tissue. When iodinated contrast medium is used, numerous pharmacokinetic and physiological interactions affect contrast attenuation.[1-3] Patient- and injection-related factors are the 2 most important determinants of contrast attenuation. Patient-related factors include cardiovascular status, body weight, hydration status, and renal function. Variables related to contrast medium injection are of equal importance and include volume, concentration, and rate of injection. In addition, the injection protocol (ie, whether the contrast agent is infused in monophasic or multiphasic fashion or with subsequent saline flushes) affects vascular and parenchymal attenuation.[1-4]

The CT appearance of adrenal glands has been described in healthy dogs, in dogs with pituitary-dependent hyperadrenocorticism, and in dogs with primary adrenal neoplasia.[5-10] A recent study[11] compared the CT findings of 17 dogs with different types of adrenal tumors.[11] Vascular invasion was reliably identified, but distinction among tumor types was not possible on the basis of CT findings alone. However, other investigators had observed that contrast attenuation

**ABBREVIATION**

| | |
|---|---|
| HU | Hounsfield units |

of pheochromocytomas was significantly increased, compared with that of adenocarcinomas.[a,b]

To our knowledge, there have been no CT studies on the effect of injection-related factors on contrast attenuation of canine adrenal glands. Thus, the purpose of the study reported here was to investigate and compare the effects of 3 different contrast medium injection protocols on contrast attenuation of adrenal glands in healthy dogs. The 3 protocols selected included constant injection of contrast medium, exponentially decelerated injection of the same dose, and constant-rate injection of half the dose over half the time. We hypothesized that there would be a difference in peak attenuation and time to peak attenuation among the 3 protocols and, more importantly, that these differences would be identified between the full-dose constant rate injection and the full-dose decelerated rate injection. Injecting half the dose over half the time was done to examine whether injecting a lower dose over a shorter period of time would result in the same degree of attenuation as injecting a higher dose over a longer period of time. The ultimate goal was to establish a standardized protocol for CT scanning of normal adrenal glands with optimum attenuation in healthy dogs.

## Materials and Methods

### Dogs

Nine healthy sexually intact (4 males and 5 females) Beagles were used in the study. The dogs were 28 to 33 months old (median, 33 months; mean, 31 months) and weighed 9.5 to 14.8 kg (median, 14 kg). All dogs were considered healthy on the basis of results of physical examination, CBC, serum biochemical analysis, and urinalysis. The dogs were housed at a university facility in standard kennels in groups of 2 to 4, fed dry adult maintenance dog food, and had access to water ad libitum. All procedures were approved by the Cantonal Veterinary Office of Zurich (permission No. TVB 186/2012) and conducted in accordance with guidelines established by the Animal Welfare Act of Switzerland.

### Procedures

A randomized crossover study design was used. Each dog was assigned an identification number by an investigator drawing its name from a bag and then drawing a number (1 to 9) from another bag. The order of the injection protocols for each dog was determined by drawing the sequence from a third bag. Each dog underwent each of the 3 IV contrast medium injection protocols: the full dose (700 mg of iodine/kg) delivered at a constant rate over 20 seconds (full-dose constant rate), the same dose delivered by an exponentially decelerated injection method over 20 seconds (full-dose decelerated rate), and one-half of the full dose (350 mg of iodine/kg) delivered at a constant rate over 10 seconds (half-dose constant rate). For the exponential decay curve ($y = a \bullet e^{-t/\tau} + b$),[12,13] where y is the injection rate, a is the initial injection rate – b, e is a numerical constant equal to 2.71828 (Euler number), t is time after the start of injection, $\tau$ is tan (exponential time constant), and b is the approximated final injection rate, the parameters were set at a = 5, b = 0.63, and $\tau$ = 4 (these values were chosen empirically to result in an injection curve with a reasonable decay over the injection time). The half-life $\lambda$ was calculated as $^1/\tau$. The area under the injection curve represented the dose of contrast medium expressed as $F(t) = \int a \bullet e^{-t/\tau} + b\ dt$, where F(t) is the amount of contrast medium injected at the time point t, t is time after the start of injection, and dt represents the differential of the function. For a given injection time t1, this formula becomes $F(t1) = a\ \tau\ (1 - e^{-t1/\tau}) + bt1$ and is thus used to calculate the applicable dose. The injection was divided into 6 steps: 3 steps covered $\tau$, and the other 3 steps were distributed equally over the remaining injection time **(Figure 1)**. Each dog received the 3 different injection protocols 7 days apart. The washout period was determined on the basis of study results regarding pharmacokinetics and biodistribution of iodinated contrast agents in humans and healthy dogs.[14,15]

All dogs received acepromazine maleate[c] (0.03 mg/kg, IM) and methadone hydrochloride[d] (0.5 mg/kg, IM) as premedication. After approximately 20 to 30 minutes, the hair was clipped from the dorsal aspect of a forelimb, an IV catheter was aseptically placed in the cephalic vein, and propofol[e] (4 mg/kg, IV) was injected to allow endotracheal intubation. The

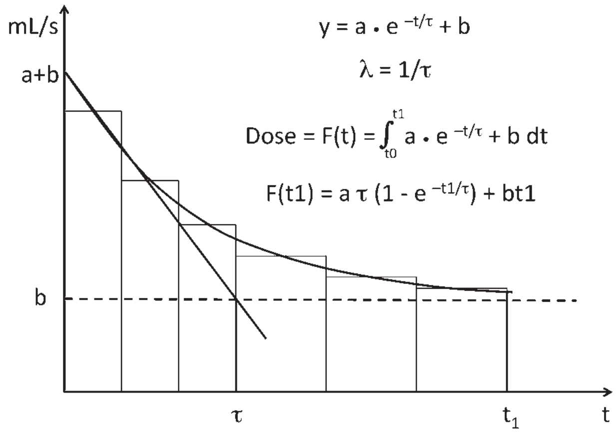


**Figure 1**—Schematic illustration of the exponential decay curve injection method described by the mathematical equation $y = a \bullet e^{-t/\tau} + b$, where y is injection rate, a is the initial injection rate – b, e is a numerical constant equal to 2.71828 (Euler number), t is time after the start of injection, $\tau$ is tan (exponential time constant), and b is the approximated final injection rate. The half-life $\lambda$ is calculated as $^1/\tau$. The area under the curve represents the contrast medium dose expressed as $F(t) = \int a \bullet e^{-t/\tau} + b\ dt$, where F(t) is the amount of contrast medium injected at the time point t, t is time after start of injection, and dt represents the differential of the function. For a given injection time t1, this formula becomes $F(t1) = a\ \tau\ (1 - e^{-t1/\tau}) +$ bt1 and thus calculates the applicable dose. The injection was divided into 6 steps: 3 steps covered $\tau$ and the other 3 steps were distributed equally over the remaining injection time.

dogs were then connected to a semiclosed circle system and mechanically ventilated throughout the study period. Anesthesia was maintained with sevoflurane[f] in oxygen. A multiparameter monitor was used to record heart rate, respiratory rate, body temperature, peripheral oxygen saturation, arterial blood pressure (noninvasive method), inspiratory and expiratory oxygen concentrations, end-tidal $CO_2$ concentration, and sevoflurane concentration. The dogs were positioned in dorsal recumbency for the CT scans, and transient apnea was induced for every scan by administration of a rocuronium bromide[g] bolus (0.3 mg/kg, IV) and momentary suspension of mechanical ventilation (duration, ≤ 120 seconds). All serial CT scans were conducted in a cranial-to-caudal direction from the midliver level to the level of the caudal pole of the left kidney. After an unenhanced scan, iodinated low-osmolar contrast medium[h] with a concentration of 350 mg of iodine/mL (warmed to room temperature [21°C]) was administered as described via an automatic programmable injector[i] through the cephalic venous catheter. Subsequent CT scans were carried out at the following time points (minutes:seconds) after the start of injection: 0:00, 0:15, 0:30, 0:45, 1:00, 1:15, 1:30, 2:30, 3:30, 4:30, 5:30, 6:30, 7:30, 8:30, 9:30, 10:30, 12:30, 14:30, and 16:30. Dogs were kept anesthetized until 10 minutes after contrast medium injection procedures. During that time, blood pressure and heart rate were monitored. Thereafter, dogs recovered and were routinely monitored (with temperature, heart rate, and respiratory rate assessed every 5 minutes) for another 30 minutes. Then dogs were moved to a ward under routine observation for another 12 hours until they were returned to their normal environment. Cardiovascular data (heart rate and blood pressure) and data related to adverse effects (not requiring intervention) during the study period were recorded for use in another concurrently performed study.

To ensure that peak enhancement was not missed with the described CT protocol, 4 of the 9 dogs underwent an additional CT scan with a full-dose constant rate injection protocol but with the imaging procedure revised according to the following procedure: the left adrenal gland was scanned at a single location (1 plane) every 2 seconds for 2 minutes after the start of contrast medium injection. This additional CT procedure was conducted ≥ 7 days after the previous scan.

A 16-slice CT scanning machine[j] was used with the following settings: voltage peak, 120 kVp; current, 250 mA; pitch, 0.688; rotation time, 0.75 seconds; and detector collimation, 16 × 0.75 mm. The raw data were reconstructed in a soft tissue algorithm with an increment of 0.5 mm and a matrix of 512 × 512 pixels. The images were exported to a workstation[k] and reviewed with a window width of 600 and window level of 150 by one of the authors (AB) who was not blinded to treatment group and who worked under regular (daily) supervision of a board-certified radiologist (MD).

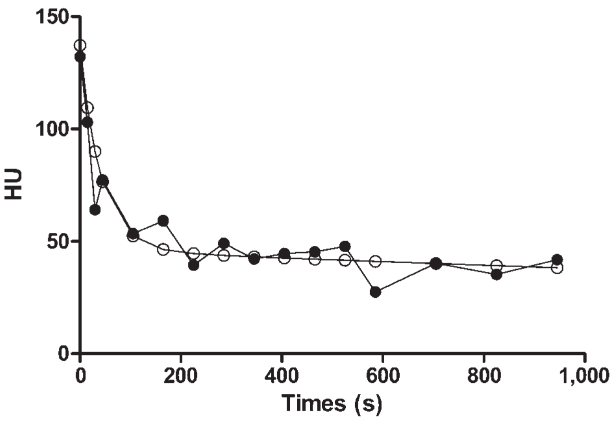


**Figure 2**—Graphic image depicting washout of iodinated contrast medium in a healthy Beagle following administration of the agent with a full-dose constant rate injection protocol. Closed circles represent the measured values, and open circles represent the estimated values.

## Measurement techniques

To quantify attenuation, a slice was selected in which both adrenal glands were visible but the phrenicoabdominal artery and vein were not. The contour of each adrenal gland was outlined with the closed polygon tool in the workstation software, excluding the margins, periadrenal fat, and blood vessels. The software calculated the mean and SD attenuation of the tissue within the region of interest.

Pharmacokinetic parameters were analyzed with the aid of time-attenuation curves generated by use of the workstation software. Peak attenuation and time to peak attenuation were used to evaluate distribution of the contrast medium in the adrenal glands. Fifteen to 17 measurement points were available for analysis of the washout of the contrast medium. The slopes of the curve for early ($\alpha$) and late ($\beta$) washout phases were calculated with the following pharmacokinetic equation: $c(t) = A\ e^{-\alpha \bullet t} + B\ e^{-\beta \bullet t}$, where c(t) is opacity (measured in HU) as a function of time; A and B are derived from the rate constants, the volume of distribution, and the dose administered; $\alpha$ and $\beta$ are functions of the pharmacokinetic rate constants describing distribution and excretion of the contrast medium, respectively; and t is the time after start of injection[15] **(Figure 2)**.

## Statistical analysis

To determine the number of dogs required for an acceptable probability of finding an effect of the injection method, a power analysis ($\alpha = 0.05$; $\beta = 0.9$) was conducted after the investigation of the first 6 dogs by means of a freely available software program.[l] At least 6 dogs were required to provide a statistical power of 90%, and it was determined that 9 dogs should be included in the study to ensure that ≥ 6 complete data sets were available for statistical analysis. Commercial software[m,n] was used to perform nonparametric tests for statistical analysis, and results were expressed as median and range. The Wilcoxon rank sum test was used to analyze differences in attenuation values between the left and right adrenal glands. Differences between injection protocols were tested by the Friedman test and the Dunn posttest. Differences were considered significant at $P < 0.05$.

## Results

All dogs were recovered following anesthesia. No serious immediate or delayed reactions to the contrast medium administration (ie, response requiring an intervention) occurred during the study.

### Peak attenuation and time to peak attenuation

Attenuation values did not differ between the left and right adrenal glands in the unenhanced scan ($P = 0.15$) or in scans performed with the full-dose constant rate injection ($P = 0.82$), with the full-dose decelerated rate injection ($P = 1.0$), or with the half-dose constant rate injection ($P = 0.57$). The values for the left and right adrenal glands were therefore combined for further analysis.

For the full-dose constant rate injection, peak attenuation for combined (left and right) adrenal glands was 129 HU (range, 90.1 to 152.3 HU) and time to peak attenuation was 30 seconds (range, 15 to 45 seconds); for the full-dose decelerated rate injection, the values were 132.5 HU (range, 99.4 to 172 HU) and 23 seconds (range, 15 to 30 seconds), respectively; and for the half-dose constant rate injection, the values were 86.95 HU (range, 55.3 to 103.9 HU) and 15 seconds (range, 15 to 30 seconds), respectively. Peak attenuation for unenhanced CT scans was 18.1 HU (range, 11.7 to 22.7 HU). Peak attenuation differed significantly between unenhanced CT scans and scans performed with the full-dose constant rate, full-dose decelerated rate, and half-dose constant rate injection protocols ($P < 0.001$, $< 0.001$ and $< 0.05$, respectively; **Figure 3**). This variable also differed significantly between the full-dose constant rate and half-dose constant rate ($P < 0.001$) and between the full-dose decelerated rate and half-dose constant rate ($P < 0.001$), but not between the full-dose constant rate and full-dose decelerated rate injection protocols. There was no significant (Friedmann test, $P < 0.03$; Dunn multiple comparisons test, $P > 0.05$) difference in time to peak attenuation among the full-dose constant rate, full-dose decelerated rate, and half-dose constant rate protocols.

For the additional CT scan of left adrenal glands performed with full-dose constant rate injection and the revised imaging protocol (every 2 seconds for 2 minutes; n = 4 dogs), peak attenuation was 160.15 HU (range, 97.9 to 175.6 HU; **Figure 4**). The time to peak attenuation in this experiment was 35 seconds (range, 28 to 40 seconds).

### Time-attenuation curves during washout

The slopes of the curve for early (α) and late (β) washout phases of contrast medium following use of the full-dose constant rate, full-dose decelerated rate, and half-dose constant rate injection protocols were summarized **(Table 1)**. The slopes of the early and late washout phases did not differ among injection protocols.

## Discussion

Injection-related variables including iodine concentration, injection rate, duration of injection, and injection protocol are important factors that affect the timing and degree of attenuation in contrast-enhanced CT examinations.[1-4] In the present study, we assessed attenuation of adrenal glands in healthy dogs with and without contrast medium administration by 1 of 3 protocols: full-dose constant rate injection (700 mg of iodine/kg, IV, delivered at a constant rate over 20 seconds), full-dose decelerated rate injection (700 mg of

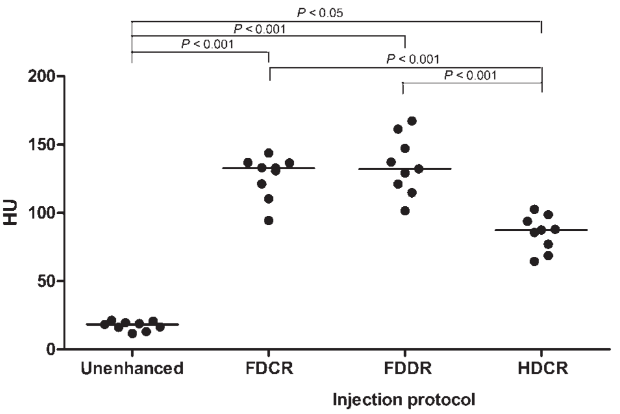


**Figure 3**—Scatterplot showing peak attenuation of adrenal glands (mean of left and right for each of 9 dogs) measured in unenhanced CT scans and scans performed with full-dose constant rate (FDCR; 700 mg of iodine/kg, IV, at a constant injection rate over 20 seconds), full-dose decelerated rate (FDDR; 700 mg of iodine/kg, IV, following an exponential decay curve over 20 seconds), and half-dose constant rate (HDCR; 350 mg of iodine/kg, IV, at a constant rate over 10 seconds) contrast medium injection protocols. The horizontal lines depict the median of 9 measurements.

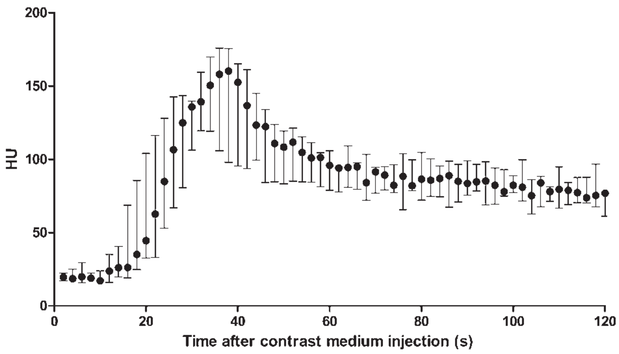


**Figure 4**—Median and range attenuation of left adrenal glands in 4 dogs over time after injection of contrast medium with the full-dose constant rate injection protocol. For this experiment, the imaging protocol was revised to scan 1 adrenal gland/dog in a single plane every 2 seconds over a 2-minute period. Times were measured from the start of contrast medium injection.

**Table 1**—Median (range) slopes of the curve for early (α) and late (β) washout phases of iodinated contrast medium administered by means of 1 of 3 protocols to 9 healthy Beagles in a study to assess the effects of contrast medium injection technique on attenuation values of canine adrenal glands during contrast-enhanced CT.

| | Washout phase | |
|---|---|---|
| | α ($s^{-1}$) | β ($s^{-1}$) |
| Full-dose constant rate | −0.0157 (−0.0354 to −0.0088) | −0.0004 (−0.0008 to −0.00005) |
| Full-dose decelerated rate | −0.0159 (−0.0226 to −0.0101) | −0.0004 (−0.0007 to −0.00005) |
| Half-dose constant rate | −0.0187 (−0.0364 to −0.0095) | −0.0003 (−0.0007 to −0.0001) |

The full-dose constant rate and full-dose decelerated rate injection protocols required IV administration of 700 mg of iodine/kg (total dose) at a constant injection rate over 20 seconds or at a rate following an exponential decay curve over 20 seconds, respectively. The half-dose constant rate injection protocol required IV administration of a volume calculated to deliver 350 mg of iodine/kg at a constant rate over 10 seconds.

iodine/kg, IV, at a rate following an exponential decay curve over 20 seconds), and half-dose constant rate injection (350 mg of iodine/kg, IV, at a constant rate over 10 seconds). Peak attenuation was significantly associated with the dose of contrast medium used. Of note, the time to peak enhancement was not significantly affected by the injection protocol. It is known that the contrast medium dose or volume affects peak attenuation; the degree of contrast attenuation increases at a rate proportional to the amount of iodine deposited in a target organ or intravascular blood volume.[1–3,16] Because injection duration (volume divided by injection rate) also affects attenuation values, we investigated whether injecting a lower dose in a shorter time had the same effect as injecting a higher dose over a longer time. Interestingly, peak attenuation was significantly decreased when the lower contrast medium dose was used, even though it was administered in half the time. This was most likely attributable to the fact that the injection rates of both protocols were the same (2 mL/kg/20 s for the full-dose constant rate injection vs 1 mL/kg/10 s for the half-dose constant rate injection). Shortening the injection duration without increasing the injection rate results in the administration of a smaller contrast medium volume and thus a proportional decrease in the magnitude of vascular and parenchymal attenuation.[1]

Time to peak attenuation is another factor that was shown to be affected by the duration of contrast medium injection in CT examination of the pulmonary arteries, aorta, and liver of humans[1,2] and dogs.[17,18] Short injection duration resulted in a short time to peak attenuation and prolonged injection duration in a later time to peak attenuation of the contrast medium.[1,2,17,18] However, to our knowledge, effects of injection protocols on this variable have not previously been evaluated for the adrenal glands of any species. We expected time to peak attenuation to be shorter in dogs following the half-dose constant rate injection (duration of 10 seconds) than in the same dogs following the full-dose constant rate injection (duration of 20 seconds), but there was no significant difference in this variable between the 2 protocols. It is possible that the total iodine administration rate, referred to as iodine flux and calculated by multiplying the contrast injection rate by the iodine concentration, is a more crucial determinant of time to peak attenuation than the injection duration.[2] In the present study, the contrast injection rate (2 mL/kg/20 s or 1 mL/kg/10 s) and the iodine concentration (350 mg/mL) were the same in both injection protocols, which could have diminished the effect of the injection duration on time to peak attenuation.

One goal of this study was to investigate whether attenuation values for canine adrenal glands would differ between constant rate and exponentially decelerated injection methods. The exponential deceleration method was complex, required considerable calculation, and seemed prone to error, but the attenuation values for adrenal glands of healthy dogs did not differ between the 2 methods. In humans, vascular attenuation values were more uniform when the exponentially decelerated injection method was used for CT angiography[19]; however, parenchymal attenuation was not studied. Whether attenuation values would differ between these methods in more highly vascularized tissue should be evaluated.

The timing and duration of scanning are crucial factors in contrast-enhanced CT because of the need to coordinate image acquisition with the times when contrast attenuation is most informative. Peak attenuation is easily missed if the timing is not optimal. In the present study, peak attenuation of the adrenal glands in healthy dogs was detected approximately 30 seconds after contrast injection (with median values for the 3 contrast injection protocols ranging from 15 to 30 seconds). However, the ideal interval between injection and CT image acquisition in dogs with adrenal gland disease has not been established, and given the variable findings of other investigators in regard to the usefulness of this modality to distinguish among adrenal tumor types,[11,a,b] further CT studies of dogs with adrenal disease are needed to investigate the utility of specific attenuation values in this tissue for diagnostic purposes. Attenuation on postcontrast images has not been shown to allow reliable differentiation of benign and malignant adrenal lesions in humans.[20–22] However, adrenal adenomas lose contrast attenuation more rapidly than malignant adrenal masses because of differences in vascular permeability and density, and the percentage washout of the contrast medium on delayed images (at 15 minutes after contrast administration) is a reliable indicator for distinguishing between adenomas and malignant masses in humans.[20–22] To our knowledge, washout parameters of adrenal masses have not been evaluated in veterinary medicine, but our results indicated that under physiologic conditions, the washout of the contrast medium from healthy adrenal glands is exponential and independent of dose or injection protocol within the tested ranges. This finding was expected, considering that, following IV administration, iodinated contrast medium is distributed from the vascular to the extravascular space while being continuously excreted by the kidneys.[2]

The viscosity of the nonionic, low-osmolar contrast medium used in the present study is affected by temperature, and it is lower at higher temperatures.[23] Therefore, warming the contrast medium reduces viscosity and increases the efficiency of its delivery through a catheter, which may influence attenuation values.[23] We used contrast medium warmed to room temperature; whether warming the contrast medium to the dogs' body temperature would lead to different results is not known. Although no adverse effects that required intervention occurred during the study, it should be noted that the study population was small, all dogs were healthy young adult Beagles.

The relatively small number of dogs (as dictated by the Animal Welfare Act of Switzerland) in the study limited the power of statistical tests. However, we performed a power analysis and determined that the minimum number of dogs required for an acceptable probability (6 dogs for a statistical power of 90%) of finding an effect of the injection method was met. The study had other shortcomings, one being that it was an experimental study with results that can be related only to healthy dogs without evidence of adrenal gland disease or other illnesses, and another being failure to blind the investigator that performed CT image analysis to the treatment of dogs. Additionally, the experimental CT model consisting of repetitive scanning of the whole adrenal gland every 15 seconds (as in the first 1.5 minutes for each dog in this study) is not clinically feasible but was done in an effort to generate information about the volume of the adrenal glands. Nonetheless, our results provide useful information about the pharmacokinetics of contrast medium in the adrenal glands of healthy dogs.

Our findings supported that the dose of contrast medium and the timing of postinjection CT scanning are the main determinants of peak attenuation for adrenal glands in healthy dogs, whereas the effects on attenuation of the 3 contrast medium injection protocols tested were of minor importance. The exponentially decelerated injection method was complex and not user-friendly, required considerable calculation, and seemed therefore prone to error. A constant rate injection protocol delivering a total dose of 700 mg of iodine/kg over 20 seconds and scans obtained approximately 30 seconds after the start of contrast injection provided images with maximum adrenal gland attenuation values in healthy dogs.


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The authors declare that there were no conflicts of interest.


## Footnotes

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# Curriculum Vitae

**Personalien**

| | |
|---|---|
| Vorname Name | Alexandra Blaser |
| Geburtsdatum | 2. April 1985 |
| Geburtsort | Wettingen |
| Nationalität | Schweizerin |
| Heimatort bei Schweizern | Langnau im Emmental, BE |

**Ausbildung**

| | |
|---|---|
| 08/1992 – 08/1997 | Primarschule, Ennetbaden, Schweiz |
| 08/1997 – 08/2001 | Bezirksschule, Baden, Schweiz |
| 08/2001 – 06/2005 | Kantonsschule, Baden, Schweiz |
| 06/2005 | Matura, Kantonsschule, Baden, Schweiz |
| 08/2007 – 01/2013 | Studium Veterinärmedizin, Vetsuisse-Fakultät Universität Zürich, Zürich, Schweiz |
| 01/2013 | Staatsexamen zur Eidg. Dipl. Tierärztin med. vet., Vetsuisse-Fakultät Universität Zürich, Schweiz |

**Dissertation**

| | |
|---|---|
| 03/2013 – 09/2016 | Anfertigung der Dissertation unter der Leitung von Prof. Dr. med. vet. Nadja Sieber-Ruckstuhl, am Departement für Kleintiere, Klinik für Kleintiermedizin der Vetsuisse-Fakultät Universität Zürich, Schweiz, Direktorin: Prof. Dr. Claudia Reusch |

**Berufliche Tätigkeiten**

| | |
|---|---|
| 06/2013 – 06/2014 | Assistentin am Departement für Kleintiere, Intensivstation, Vetsuisse-Fakultät Universität Zürich, Schweiz |
| 07/2014 – 03/2015 | Assistentin für Kleintiere, Tierklinik Masans, Chur, Schweiz |
| 04/2015 - | Assistentin am Departement für Kleintiere, Kleintiermedizin, Vetsuisse-Fakultät Universität Zürich, Schweiz |